A1 cont'd

36. The method according to claim 33 wherein the influenza virus antigen preparation is selected from the group consisting of split virus antigen preparations, subunit antigens, chemically or otherwise inactivated whole virus.

37. The method according to claim 36 wherein the influenza antigen preparation is a split virus antigen preparation.

38. The method according to claim 33 wherein the formulation comprises at least one surfactant.

39. The method according to claim 38 wherein the surfactant is at least one non-ionic surfactant selected from the group consisting of the octylphenoxypolyethoxyethanols (for example from the commercially available Triton ™ series), polyoxyethylene sorbitan esters (Tween ™ series) and polyoxythylene ethers or esters of general formula (I):

(I) $HO(CH_2CH_2O)_n$-A-R

wherein n is 1-50, A is a bond or –C(O)-, R is C_{1-50} alkyl or phenyl C_{1-50} alkyl, and combinations of two or more of these.

40. The method according to claim 39 wherein the non-ionic surfactant is at least one surfactant selected from the group consisting of t-octylphenoxypolyethoxyethanol (Triton X-100), polyoxyethylene sorbitan monooleate (Tween 80) and laureth 9, or a combination of two or more of these.

41. The method according to claim 40 wherein the one-dose intranasal preparation comprises a combination of two of the three non-ionic surfactants, namely polyoxyethylene sorbitan monooleate (Tween 80) and t-octylphenoxypolyethoxyethanol (Triton X-100).

42. The method according to claim 41 wherein the one-dose intranasal preparation comprises a combination of all three non-ionic surfactants.

43. The method according to claim 33 wherein the one-dose intranasal preparation further comprises a bile acid or cholic acid, or derivative thereof such as sodium deoxycholate.

44. The method according to claim 33 wherein each dose of the vaccine formulation contains a low dose of haemagglutinin.

45. The method according to claim 44 wherein the haemagglutinin content per influenza strain is about 30 μg or less per dose.

46. The method according to claim 45 wherein the haemagglutinin content per influenza strain is about 15 μg or less per dose.

47. The method according to claim 46 in which the heamagglutinin content is about 7.5 μg or less of haemagglutinin per virus strain per vaccine dose.

48. The method according to claim 33 wherein the vaccine formulation is in a low volume per dose.

49. The method according to claim 48 wherein the volume per dose is less than 500 μl, or less than 300 μl or not more than about 200 μl per dose.

50. The method according to claim 33 wherein the one-dose intranasal preparation is delivered in a bi-dose format of two sub-doses.

51. The method according to claim 33, wherein the one-dose intranasal preparation does not contain an added immunostimulant.

52. The method according to claim 33, wherein the one-dose intranasal preparation further comprises a non-toxic derivative of lipid A, preferably selected from non-toxic derivatives of monophosphoryl lipid A and diphosphoryl lipid A.

53. The method according to claim 52, wherein the one-dose intranasal preparation comprises 3D-MPL.

54. The method according to claim 53, wherein the one-dose intranasal preparation comprises 3D-MPL and laureth 9.

A1 cont'd

55. A method for prophylaxis of influenza infection or disease in a subject which method comprises administering to the subject a single dose of a non-live influenza virus vaccine via a mucosal surface to induce an immune response which meets at least two of the following criteria for all strains of influenza present in the vaccine:

(i) a seroconversion rate of greater than or equal to 40%;

(ii) a seroprotection rate of greater than or equal to 70%; and

(iii) a conversion factor of greater than or equal to 2.5.

56. A method for prophylaxis of influenza infection or disease in a subject which method comprises administering to the subject a single dose of a low HA, non-live influenza virus vaccine via a mucosal surface to induce an immune response which meets at least two of the following criteria for all strains of influenza present in the vaccine:

(i) a seroconversion rate of greater than or equal to 40%;

(ii) a seroprotection rate of greater than or equal to 70%; and

(iii) a conversion factor of greater than or equal to 2.5.

57. The method according to claim 55 or claim 56 wherein all three of the criteria are met for all strains of influenza present.

58. The method according to claim 55 or claim 56 wherein the one-dose vaccine is delivered intranasally.

59. A pharmaceutical kit comprising an intranasal delivery device and a one-dose vaccine which comprises a non-live influenza virus antigen preparation without an added immunostimulant.

60. A pharmaceutical kit comprising an intranasal delivery device and a one-dose influenza vaccine which generates an immune response that meets the international regulatory requirements for an influenza vaccine.

All cont'd

61. A pharmaceutical kit comprising an intranasal delivery device and a one-dose vaccine which comprises a low HA dose of a non-live influenza virus antigen preparation.

62. The pharmaceutical kit according to any one of claims 59 to 61 wherein the device is a bi-dose delivery device for delivering two sub-doses in a single administration.

63. The pharmaceutical kit according to any one of claims 59 to 61 wherein the device is an intranasal spray device.

64. A method of manufacturing an influenza vaccine for nasal application which method comprises:

(i) providing a split influenza virus preparation produced essentially as for a conventional injected influenza vaccine and comprising at least one non-ionic surfactant;

(ii) optionally adjusting the concentration of the haemagglutinin and/or the concentration of non-ionic surfactant in the preparation;

(iii) filling an intranasal delivery device with a vaccine dose from the split influenza virus preparation, said dose being a suitable volume for intranasal administration, optionally in a bi-dose format.

REMARKS

The above-identified application is being entered into the National Phase from PCT application no. PCT/EP00/09367.